REMARKS

I. Amendments

Reconsideration of the Application is respectfully requested. Upon entry of the foregoing amendment, claims 1-20 are pending in the Application. Claims 1 and 12 are amended.

Applicants respectfully request entry of the above amendments and submit that the above amendment does not constitute new matter. Support for the amendments to the claims can be found throughout the specification (considered as a whole) and in the claims as originally filed. In particular, support for the amendment to claim 1 can be found, *inter alia*, in claim 1 as originally filed and in the specification at page 8, lines 25-27. Claim 12 is amended for antecedent basis.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

II. Claim Rejections

A. Rejection Under 35 U.S.C. § 102(b)

Claims 1, 2 and 4-8 stand rejected as being anticipated by Xu *et al.*, *J. Biological Chem* (1996) 271:24711-24719 ("the Xu reference"). This rejection is respectfully traversed.

The Examiner asserts that the Xu reference discloses a method of detecting docosahexaenoic acid ("DHA") by contacting a DHA sample with a protein having a differential binding specificity for DHA over other fatty acids, i.e. brain lipid-binding protein ("BLBP"), to detect the binding of the DHA and BLBP. *See* Office Action, p. 3. However, Xu is not directed to detection of DHA. Rather, Xu describes binding studies performed using known amounts of DHA. *See* Figure 4 (reporting that the experiments of Xu were performed (A) using either 0.1 μM DHA or 0.2 μM DHA or (B) using 10 specified concentrations of DHA in the range of 1-100 μM). Thus, Xu did not detect the presence of DHA because DHA was already known to be present in the experiments (at predetermined concentrations).

Claim 1, from which claims 2 and 4-8 depend, has been amended. Therefore, The amended claims recited that the sample tested in the claimed assay contains an unknown amount of DHA. Clearly, the experiments of Xu, which use predetermined DHA concentration, do not

anticipate the amended claims. Applicants respectfully request that the Examiner reconsider the rejections under 35 U.S.C. § 102(b) and that the rejections be withdrawn.

B. Rejections Under 35 U.S.C. § 103(a)

In the Office Action, the Examiner rejected claims 3 and 9 as allegedly being unpatentable over the Xu reference in view of U.S. Patent No. 6,326,159, issued to Ullman *et al.* ("the Ullman patent"); claims 10 and 11 as allegedly being unpatentable over the Xu reference and claims 12 and 13 as being unpatentable over the Xu reference in view of U.S. Patent No. 5,447,957, issued to Adams *et al.* ("the Adams patent"). Applicants respectfully traverse these rejections.

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure.

M.P.E.P. § 2142 at 2100-128.

i. Claims 3 and 9

The Examiner asserts that the Xu reference discloses a method for detecting DHA but is silent in using a protein to detect the DHA-BLBP complex. The Examiner, further asserts that the Ullman patent discloses the use of a second antibody specifically for detecting the complex of ligand with ligand protein. Thus, the Examiner alleges it would have been obvious to one skilled in the art at the time the invention was made to combine the method of the Xu reference with the complex-specific antibody in the Ullman patent. *See* Office Action, p. 4.

First, the Examiner did not address Applicants' argument in the Response filed on January 21, 2005 with regard to the obviousness rejection of claim 3 in the previous non-final Office Action, which is now also applicable to the obviousness rejection of claim 9. To reiterate, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the Xu reference and the

Ullman patent. Furthermore, one of ordinary skill in the art would not be motivated to combine the references because the Xu reference discloses an experimental determination of binding affinity, not a detection assay, and the Ullman patent discloses an immunoassay wherein binding affinity is already known. It is Applicants' disclosed detection assay that makes the combination obvious, but Applicants' disclosure cannot be used to provide motivation to combine the references. *See* M.P.E.P. § 2145 at 2100-161.

Second, even if the Ullman patent and the Xu reference were combined, the combination would not produce the present invention. As stated above, the Xu reference is determining binding affinity. Use of antibodies according to Ullman in the experiments of Xu would simply produce an alternative method of measuring binding affinity in samples with predetermined DHA concentration. The combination does not provide any teaching to select samples with undetermined DHA content.

Claims 3 and 9 are not obvious in view of the Xu reference and the Ullman patent because there is no suggestion or motivation to combine the two references, and even if the references are combined, the result would be different from the claimed invention. Therefore, Applicants respectfully request the Examiner reconsider the rejection of claims 3 and 9 under 35 U.S.C. § 103(a) and that the rejection be withdrawn.

ii. Claims 10 and 11

The Examiner states that the Xu reference is silent in using biological samples in the method described but that the Xu reference reviews the role of BLBP in the developing central nervous system and discloses the high specificity and affinity of DHA for BLBP. The Examiner reasons, therefore, that it would have been obvious to one skilled in the art to apply the method of binding BLBP and DHA in a biological sample. *See* Office Action, p. 5.

The Examiner asserts that it would be obvious to use Applicants' assay on neural tissue because of interest in neural tissue as a research field, but this assumes Applicants' invention, which is not disclosed in the prior art (as pointed out above). The only disclosure of the claimed DHA assay is in the present application, which may not be used as prior art. Therefore, the Examiner has not made a prima facie case of obviousness for the use of Applicants' assay on biological samples.

The Examiner also did not rebut Applicants' arguments presented in the Response to the previous Office Action with regard to the obviousness rejection of claims 10 and 11. As previously stated, one of ordinary skill in the art would not be motivated to use biological samples in the binding affinity study of the Xu reference, and even if one considered doing so, he/she would not have a reasonable expectation of success. First, the Xu reference takes great effort to ensure the BLBP is pure (see p. 24712, left col., first par. and Fig. 1) and uses isolated fatty acids (see p. 24711, right col., first par. under "Experimental Procedures"). Thus, one would not even consider using the method disclosed in the Xu reference for determining the binding affinity of one component in a multiple-component mixture.

Second, the method disclosed in the Xu reference would not be able to determine what, if any, fatty acid was present in a biological sample because the fatty acids detected in the Xu reference were radioactive and detected by using a scintillation counter. Therefore, one would not have a reasonable likelihood of success because a biological sample, under normal circumstances, is not radioactive.

Finally, one would not perform the binding affinity experiment of Xu if it were already known that a ligand for BLBP is DHA because the experiment would be moot. Again, it is Applicants' inventive assay that makes it obvious to use the binding affinity of BLBP and DHA to detect DHA in a biological sample.

Claims 10 and 11 are not obvious in view of the Xu reference because one of ordinary skill in the art would not be motivated to use biological samples in the method disclosed in the Xu reference, and even if one considered doing so, there would be no reasonable expectation of success. Therefore, Applicants respectfully request that the Examiner reconsider the rejection of claims 10 and 11 under 35 U.S.C. § 103(a) and that the rejection be withdrawn.

iii. Claims 12 and 13

The Examiner acknowledges that the Xu reference is silent regarding the use of hydrolyzing agents to release DHA from lipids for analysis. The Examiner asserts, on the other hand, that the Adams patent does teach the use of KOH, a non-enzymatic agent, to release a fatty acid from a lipid complex for identification and quantitation. Therefore, the Examiner claims it would have been obvious to one of ordinary skill in the art to use KOH to release the DHA from

the lipid complex of a sample for better purity and detection efficiency in the method disclosed in the Xu reference. *See* Office Action, p. 5.

However, the passage cited by the Examiner regarding the use of KOH to remove fatty acids from complex lipids is described in a "method for assessing the ability of a compound to alter arachidonate content of cellular phospholipids." *See* the Adams patent, col. 27, ll. 54-56. Clearly, one of ordinary skill in the art would not be motivated to use a step of the aforementioned method in the binding affinity study of the Xu reference, and even if they did so, one would not have a reasonable expectation of success.

Claims 12 and 13 are not obvious in view of the Xu reference and the Adams patent because one of ordinary skill in the art would not be motivated to use a procedure in an unrelated method in the binding affinity study disclosed in the Xu reference, and even if one considered doing so, there would be no reasonable expectation of success. Therefore, Applicants respectfully request that the Examiner reconsider the rejection of claims 12 and 13 under 35 U.S.C. § 103(a) and that the rejection be withdrawn.

REQUEST FOR CHANGE OF ATTORNEY DOCKET NUMBER

Please change the attorney docket number in the above-referenced application from 031676.0208 to **62611.000167**.

CONCLUSION

It is believed that no additional fees are due in connection with this paper. However, should the USPTO determine that a variance exists between the debit amount authorized above and the amount due, the Commissioner is hereby authorize to debit or credit any variance to the undersigned's Deposit Account No. 50-0206.

Applicant respectfully submits that this application is in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe anything further is desirable in order to place the Application in even better condition for allowance, the Examiner is invited to contact the Applicant's undersigned representative.

Respectfully submitted,
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